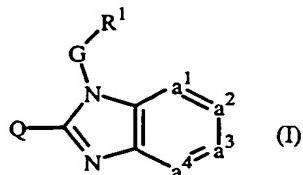


Claims

1. A compound of formula

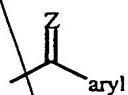


Solv 5 a prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof wherein

-a¹=a²-a³=a⁴- represents a bivalent radical of formula

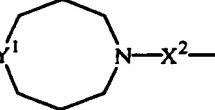
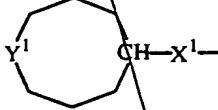
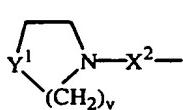
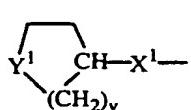
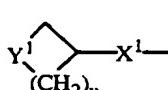
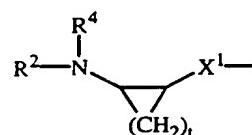
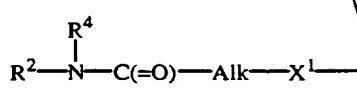
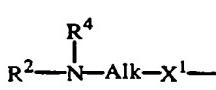
- CH=CH-CH=CH- (a-1);
- N=CH-CH=CH- (a-2);
- CH=N-CH=CH- (a-3);
- CH=CH-N=CH- (a-4); or
- CH=CH-CH=N- (a-5);

10 wherein each hydrogen atom in the radicals (a-1), (a-2), (a-3), (a-4) and (a-5) may optionally be replaced by halo, C₁₋₆alkyl, nitro, amino, hydroxy, C₁₋₆alkyloxy, polyhaloC₁₋₆alkyl, carboxyl, aminoC₁₋₆alkyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, hydroxyC₁₋₆alkyl, or a radical of formula



15 wherein =Z is =O, =CH-C(=O)-NR^{5a}R^{5b}, =CH₂, =CH-C₁₋₆alkyl, =N-OH or =N-O-C₁₋₆alkyl;

20 Q is a radical of formula



wherein Alk is C₁₋₆alkanediyl;

Y¹ is a bivalent radical of formula -NR²- or -CH(NR²R⁴)-;

25 X¹ is NR⁴, S, S(=O), S(=O)₂, O, CH₂, C(=O), C(=CH₂), CH(OH), CH(CH₃), CH(OCH₃), CH(SCH₃), CH(NR^{5a}R^{5b}), CH₂-NR⁴ or NR⁴-CH₂;

-85-

~~X² is a direct bond, CH₂, C(=O), NR⁴, C₁₋₄alkyl-NR⁴, NR⁴-C₁₋₄alkyl;~~

~~t is 2, 3, 4 or 5;~~

~~u is 1, 2, 3, 4 or 5;~~

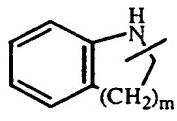
~~v is 2 or 3; and~~

5 whereby each hydrogen atom in Alk and the carbocycles and the heterocycles defined in radicals (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8) may optionally be replaced by R³; with the proviso that when R³ is hydroxy or C₁₋₆alkyloxy, then R³ can not replace a hydrogen atom in the α position relative to a nitrogen atom;

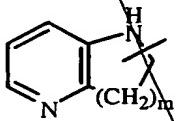
G is a direct bond or C₁₋₁₀alkanediyl optionally substituted with one, two or three

10 substituents selected from hydroxy, C₁₋₆alkyloxy, arylC₁₋₆alkyloxy, C₁₋₆alkylthio, arylC₁₋₆alkylthio, arylcarbonyl, HO(-CH₂-CH₂-O)_n-, C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, amino, mono- or di(C₁₋₆alkyl)amino, C₁₋₆alkyloxycarbonylamino and aryl;

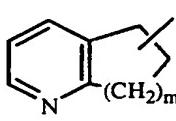
R¹ is a bicyclic heterocycle selected from quinolinyl, quinoxalinyl, benzofuranyl, 15 benzothienyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]pyridinyl, 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl or a radical of formula



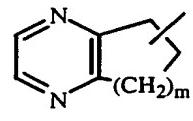
(c-1)



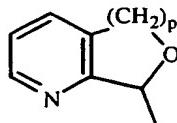
(c-2)



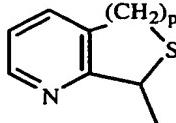
(c-3)



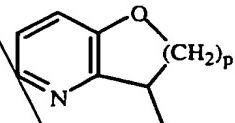
(c-4)



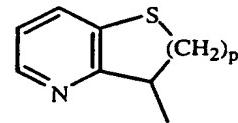
(c-5)



(c-6)



(c-7)



(c-8)

and said bicyclic heterocycles may optionally be substituted in either of the two cycles

20 with 1 or where possible more, such as 2, 3 or 4, substituents selected from halo, hydroxy, amino, cyano, carboxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkyloxy-C₁₋₆alkyl, aryl, arylC₁₋₆alkyl, arylC₁₋₆alkyloxy, hydroxyC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)-amino, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, polyhaloC₁₋₆alkyl, C₁₋₆alkylcarbonylamino, C₁₋₆alkyl-SO₂-NR^{5c}-, aryl-SO₂-NR^{5c}-, C₁₋₆alkyloxycarbonyl, -C(=O)-NR^{5c}R^{5d}, HO(-CH₂-CH₂-O)_n-, halo(-CH₂-CH₂-O)_n-, C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n- and mono- or di(C₁₋₆alkyl)amino(-CH₂-CH₂-O)_n;

25 each n independently is 1, 2, 3 or 4;
each m independently is 1 or 2;

each p independently is 1 or 2;

each R² independently is hydrogen, formyl, C₁₋₆alkylcarbonyl, Hetcarbonyl, pyrrolidinyl, piperidinyl, homopiperidinyl, C₃₋₇cycloalkyl substituted with N(R⁶)₂, or C₁₋₁₀alkyl substituted with N(R⁶)₂ and optionally with a second, third or fourth

5 substituent selected from amino, hydroxy, C₃₋₇cycloalkyl, C₂₋₅alkanediyl, piperidinyl, mono- or di(C₁₋₆alkyl)amino, C₁₋₆alkyloxycarbonylamino, aryl and aryloxy;

R³ is hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, arylC₁₋₆alkyl or arylC₁₋₆alkyloxy;

R⁴ is hydrogen, C₁₋₆alkyl or arylC₁₋₆alkyl;

R^{5a}, R^{5b}, R^{5c} and R^{5d} each independently are hydrogen or C₁₋₆alkyl; or

10 R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -(CH₂)_s- wherein s is 4 or 5;

R⁶ is hydrogen, C₁₋₄alkyl, formyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl or

C₁₋₆alkyloxycarbonyl;

15 aryl is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, polyhaloC₁₋₆alkyl, and C₁₋₆alkyloxy;

Het is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl.

2. A compound according to claim 1 wherein -a¹=a²-a³=a⁴- is a radical of formula (a-1), (a-2) or (a-3).

3. A compound according to claim 1 or 2 wherein Q is a radical of formula (b-5) wherein v is 2 and Y¹ is -NR²-.

25 4. A compound according to anyone of claims 1 to 3 wherein R² is C₁₋₁₀alkyl substituted with NHR⁶.

5. A compound according to anyone of claims 1 to 4 wherein G is a direct bond or C₁₋₁₀alkanediyl optionally substituted with one, two or three substituents selected 30 from hydroxy, C₁₋₆alkyloxy, arylC₁₋₆alkyloxy, HO(-CH₂-CH₂-O)_n-, C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n-.

6. A compound according to claim 1 wherein the compound is selected from (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-4-methyl-1-[1-(8-quinolinyl)ethyl]-1*H*-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-bromo-5,6,7,8-tetrahydro-8-quinolinyl)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-4-methyl-1*H*-benzimidazol-

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35

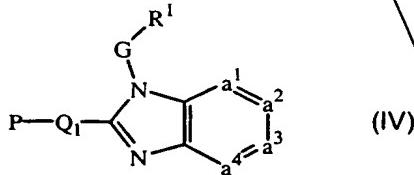
Sub A
5 2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(1-methyl-1*H*-benzimidazol-4-yl)methyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(ethoxy-8-quinolinylmethyl)-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-(5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-7-methyl-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-b]pyridin-2-amine tetrahydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-7-methyl-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-b]pyridin-2-amine

10 tetrahydrochloride monohydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(8-quinolinylmethyl)-1*H*-imidazo[4,5-c]pyridin-2-amine trihydrochloride dihydrate; *N*-[1-(2-aminoethyl)-4-piperidinyl]-4-methyl-1-(8-quinolinylmethyl)-1*H*-benzimidazol-2-amine; *N*-[1-(8-quinolinylmethyl)-1*H*-benzimidazol-2-yl]-1,3-propanediamine trihydrochloride monohydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1*H*-benzimidazol-2-amine trihydrochloride dihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(8-quinolinylmethyl)-1*H*-imidazo[4,5-b]pyridine-2-amine trihydrochloride dihydrate; (\pm)-*N*-[1-[1-(aminomethyl)-2-methylpropyl]-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-3-(2-quinolinylmethyl)-3*H*-imidazo[4,5-b]pyridin-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(1-isoquinolinylmethyl)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; *N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-3-(quinolinylmethyl)-3*H*-imidazo[4,5-b]pyridin-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-(8-quinolinylmethyl)-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-4-methyl-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(5,6,7,8-tetrahydro-2,3-dimethyl-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(3-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride monohydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(3-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-4-methyl-1*H*-benzimidazol-2-amine trihydrochloride dihydrate; (\pm)-*N*-[1-(2-

aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-4-methyl-1*H*-benzimidazol-2-amine monohydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-*c*]pyridin-2-amine trihydrochloride tetrahydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-*b*]pyridin-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-[(1-methyl-1*H*-benzimidazol-4-yl)methyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-4-methyl-1*H*-benzimidazol-2-amine; a prodrug, *M*-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof.

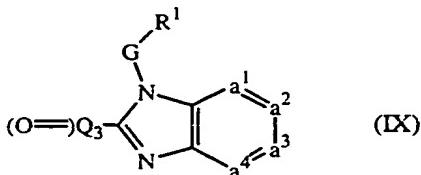
7. A compound according to any one of claims 1 to 6 for use as a medicine.
8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as described in any one of claims 1 to 6.
9. A process of preparing a composition as claimed in claim 8, characterized in that, a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as described in any one of claims 1 to 6.

10. An intermediate of formula



with R¹, G and -a¹=a²-a³=a⁴- defined as in claim 1, P being a protective group, and Q₁ being defined as Q according to claim 1 but being devoided of the R² or R⁶ substituent.

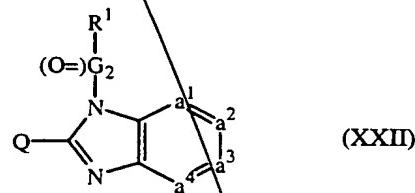
11. An intermediate of formula



-89-

~~with R¹, G and -a¹=a²-a³=a⁴- defined as in claim 1, and (O=)Q₃ being a carbonyl derivative of Q, said Q being defined according to claim 1, provided that it is devoided of the NR²R⁴ or NR² substituent.~~

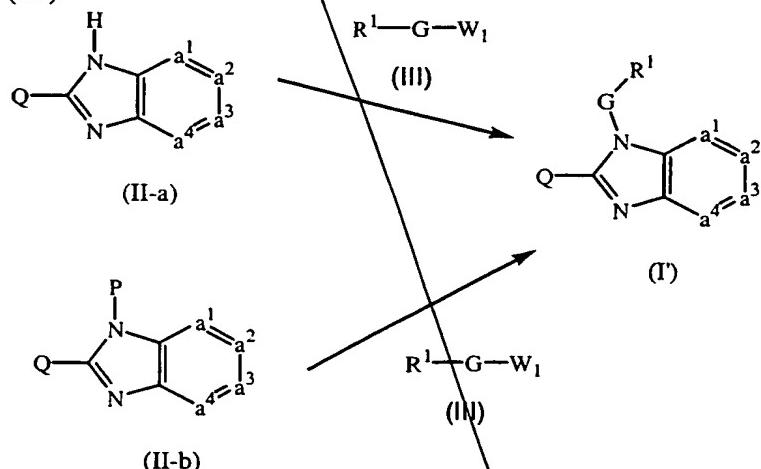
- 5 12. An intermediate of formula



~~with R¹, Q and -a¹=a²-a³=a⁴- defined as in claim 1, and (O=)G₂ being a carbonyl derivative of G, said G being defined according to claim 1.~~

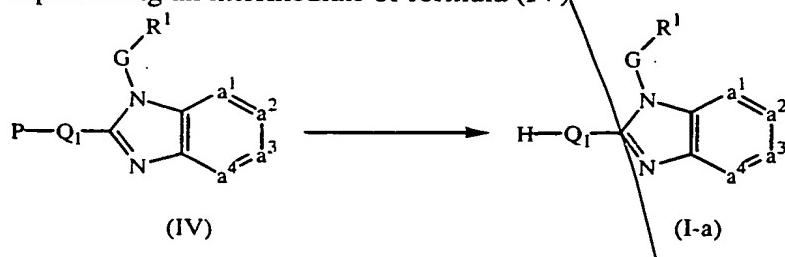
- 10 13. A process of preparing a compound as claimed in claim 1, characterized by,

- a) reacting an intermediate of formula (II-a) or (II-b) with an intermediate of formula (III)



~~with R¹, G, Q and -a¹=a²-a³=a⁴- defined as in claim 1, and W₁ being a suitable leaving group, in the presence of a suitable base and in a suitable reaction-inert solvent;~~

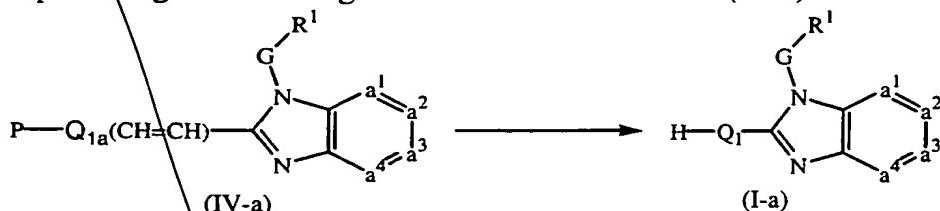
- b) deprotecting an intermediate of formula (IV)



-90-

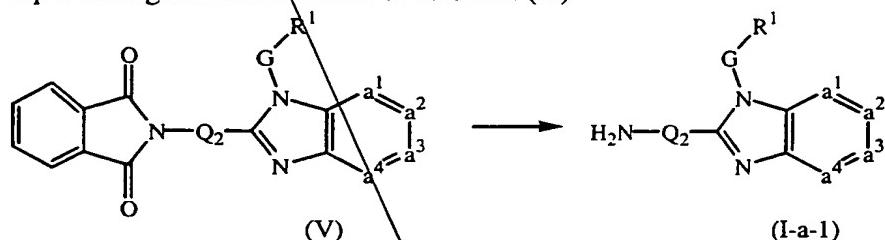
with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, H-Q₁ being defined as Q according to claim 1 provided that R² or at least one R⁶ substituent is hydrogen, and P being a protective group;

- 5 c) deprotecting and reducing an intermediate of formula (IV-a)



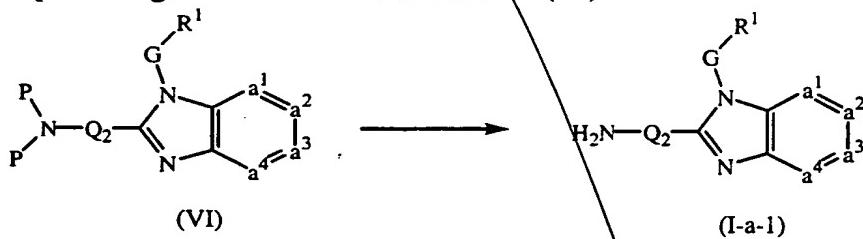
with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, H-Q₁ being defined as Q according to claim 1 provided that R² or at least one R⁶ substituent is hydrogen, Q_{1a}(CH=CH) being defined as Q₁ provided that Q₁ comprises an unsaturated bond, and P being a protective group;

- 10 d) deprotecting an intermediate of formula (V)



with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and H₂N-Q₂ being defined as Q according to claim 1 provided that both R⁶ substituents are hydrogen or R² and R⁴ are both hydrogen;

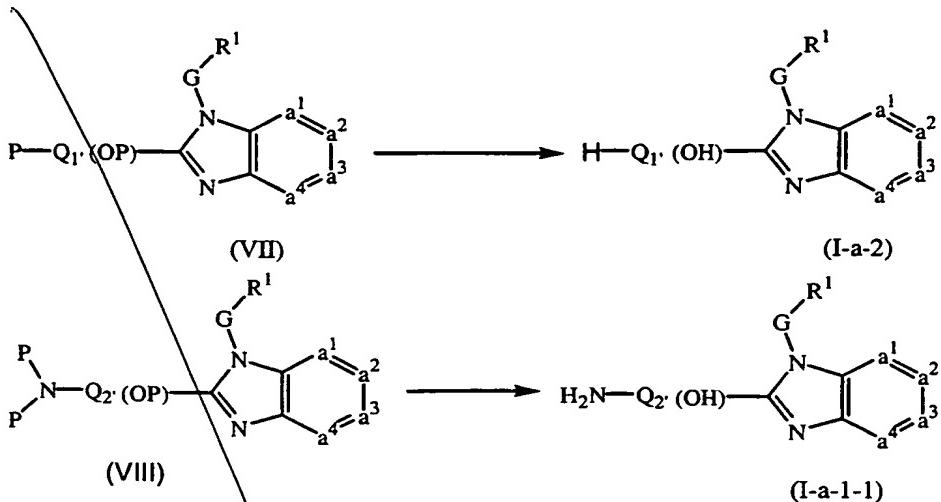
- 15 e) deprotecting an intermediate of formula (VI)



with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and H₂N-Q₂ being defined as Q according to claim 1 provided that both R⁶ substituents are hydrogen or R² and R⁴ are both hydrogen, and P being a protective group;

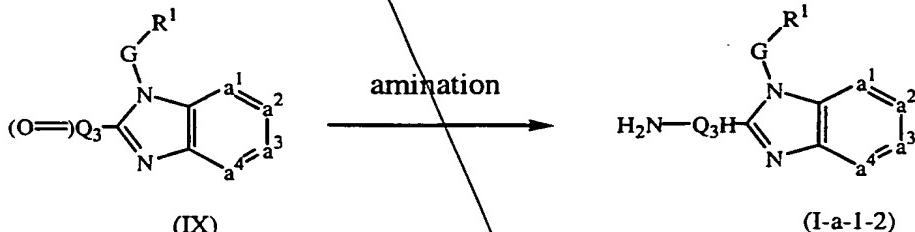
- 20 f) deprotecting an intermediate of formula (VII) or (VIII)

-91-



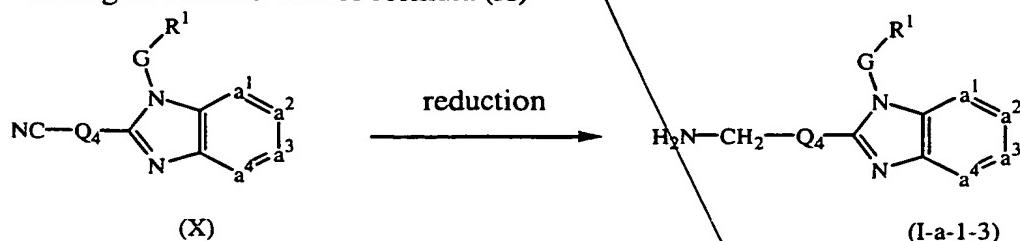
with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, H-Q₁(OH) being defined as Q according to claim 1 provided that R² or at least one R⁶ substituent is hydrogen and provided that Q comprises a hydroxy moiety, H₂N-Q₂(OH) being defined as Q according to claim 1 provided that both R⁶ substituents are hydrogen or R² and R⁴ are both hydrogen and provided that Q comprises a hydroxy moiety, and P being a protective group;

5 g) amination of an intermediate of formula (IX)



10 with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, and H₂N-Q₃H being defined as Q according to claim 1 provided that both R⁶ substituents are hydrogen or R² and R⁴ are both hydrogen, and the carbon adjacent to the nitrogen carrying the R⁶, or R² and R⁴ substituents contains at least one hydrogen, in the presence of a suitable amination reagent;

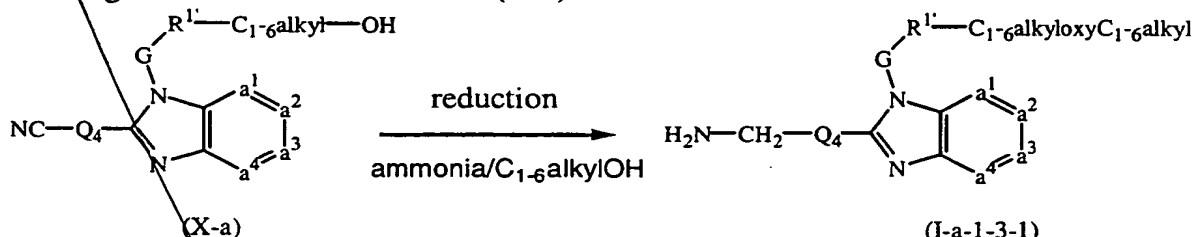
15 h) reducing an intermediate of formula (X)



-92-

with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, in the presence of a suitable reducing agent;

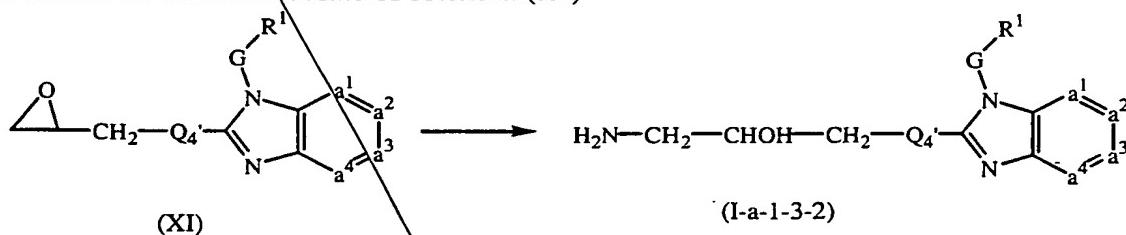
- i) reducing an intermediate of formula (X-a)



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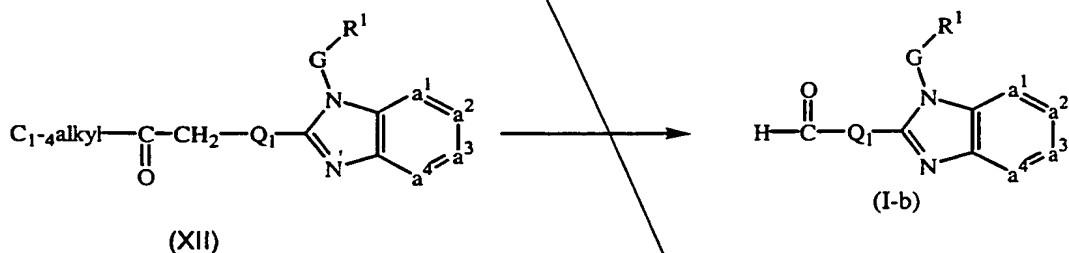
with G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, and R^1' being defined as R^1 according to claim 1 provided that it comprises at least one substituent, in the presence of a suitable reducing agent and suitable solvent;

- 10 j) amination of an intermediate of formula (XI)



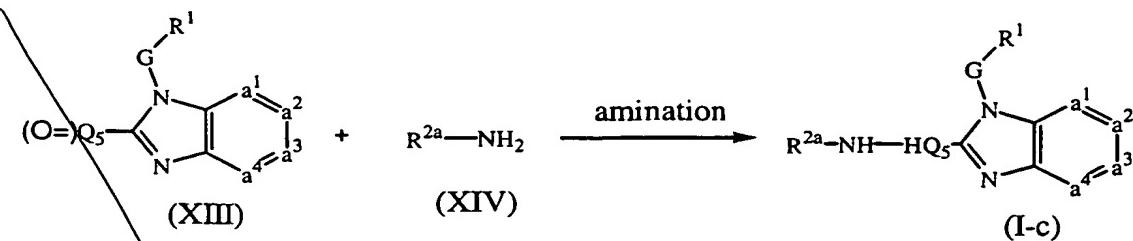
with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and $H_2N-CH_2-CHOH-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $CH_2-CHOH-CH_2-NH_2$ moiety, in the presence of a suitable amination reagent;

- 15 k) reacting an intermediate of formula (XII) with formic acid, formamide and ammonia



with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and $\text{H}-\text{C}(=\text{O})-\text{Q}_1$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is formyl;

- 20 l) amination of an intermediate of formula (XIII) by reaction with an intermediate of formula (XIV)

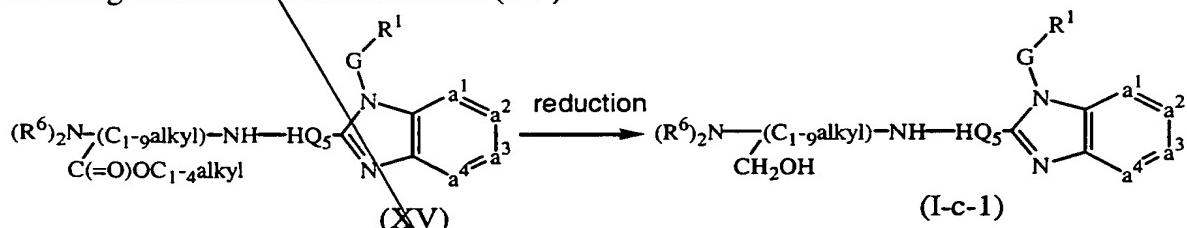


SvJ
A1

with R¹, G, and -a¹=a²-a³=a⁴ defined as in claim 1, and R^{2a}-NH-HQ₅ being defined as Q according to claim 1 provided that R² is other than hydrogen and is represented by R^{2a}, R⁴ is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R² and R⁴ substituents, carries also at least one hydrogen atom, in the presence of a suitable reducing agent;

5

- m) reducing an intermediate of formula (XV)

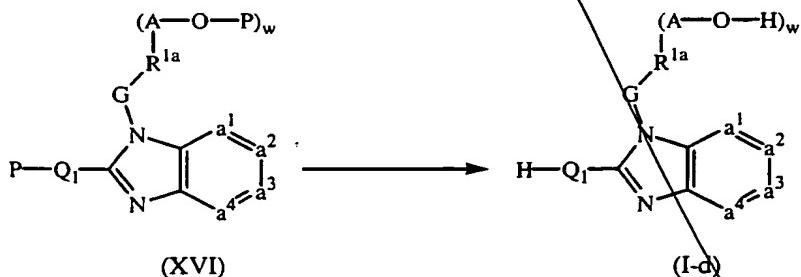


with R¹, G, and -a¹=a²-a³=a⁴ defined as in claim 1, and

(R⁶)₂N-[C₁₋₉alkyl]CH₂OH-NH-HQ₅ being defined as Q according to claim 1 provided that R² is other than hydrogen and is represented by C₁₋₁₀alkyl substituted with N(R₆)₂ and with hydroxy, and the carbon atom carrying the hydroxy, carries also two hydrogen atoms, and provided that R⁴ is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R² and R⁴ substituents, carries also at least one hydrogen atom, with a suitable reducing agent;

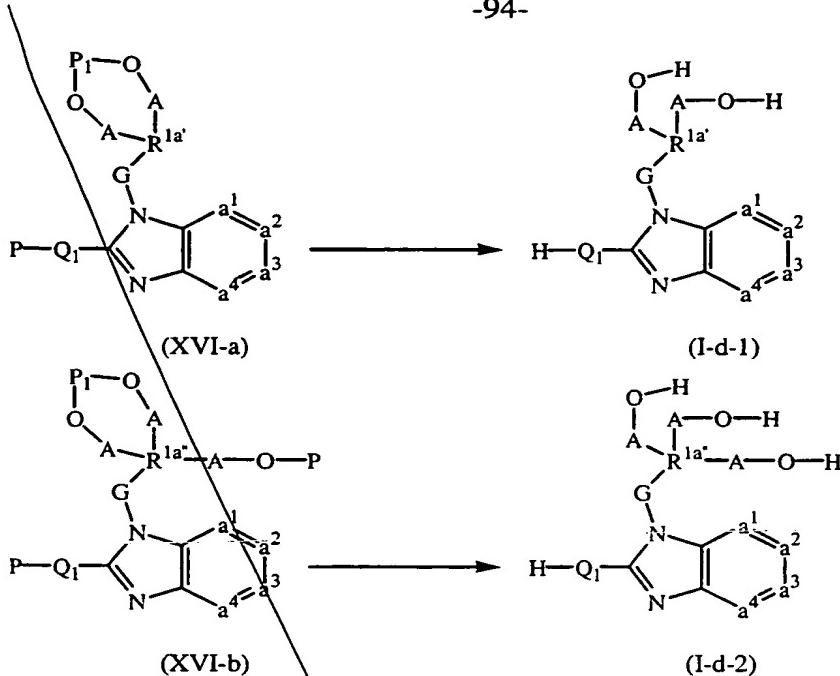
10

- n) deprotecting an intermediate of formula (XVI), (XVI-a) or (XVI-b)



-94-

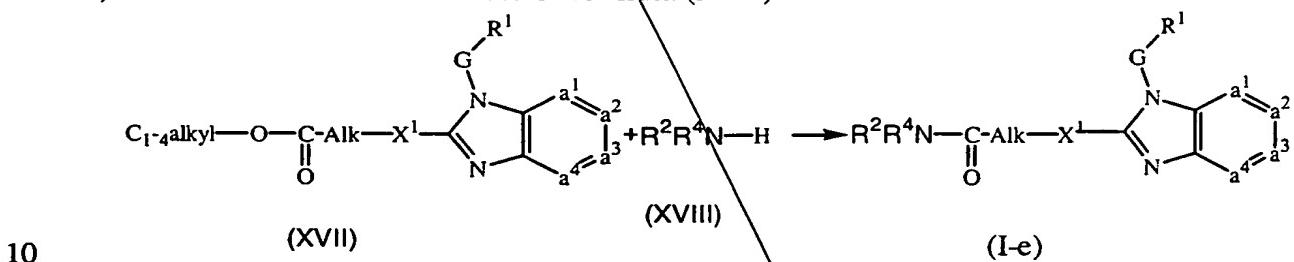
S 1
A 1



with G, and -a¹=a²-a³=a⁴- defined as in claim 1, and H-Q₁ being defined as Q according to claim 1 provided that R² or at least one R⁶ substituent is hydrogen, and R^{1a}-(A-O-H)_w, R^{1a'}-(A-O-H)₂ and R^{1a''}-(A-O-H)₃ being defined as R¹ according to claim 1 provided that R¹ is substituted with hydroxy, hydroxyC₁₋₆alkyl, or HO(-CH₂-CH₂-O)_n-, with w being an integer from 1 to 4 and P or P₁ being a suitable protecting group, with a suitable acid.

5

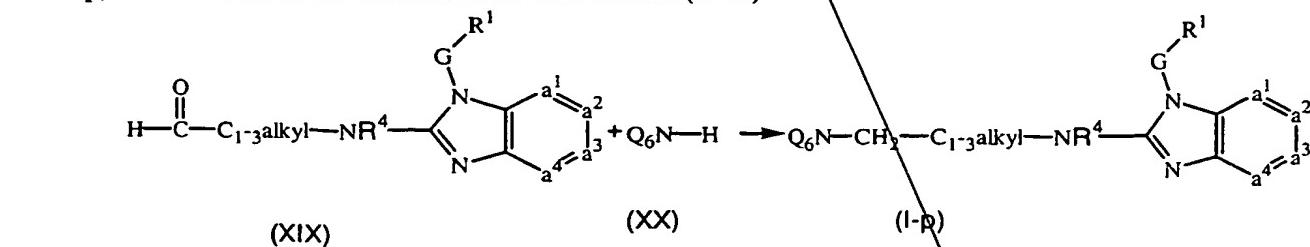
o) amination of an intermediate of formula (XVII)



10

with R¹, G, -a¹=a²-a³=a⁴-; Alk, X¹ R² and R⁴ defined as in claim 1, in the presence of a suitable amination agent;

p) amination of an intermediate of formula (XIX)

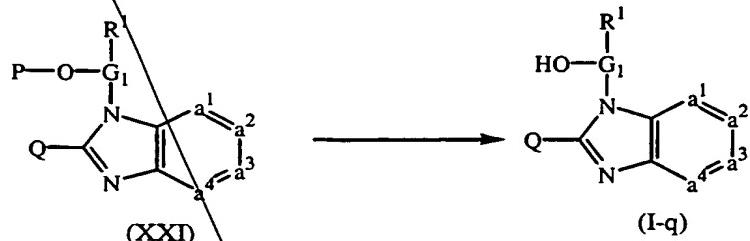


15

with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, and Q₆N-CH₂-C₁₋₃alkyl-NR⁴

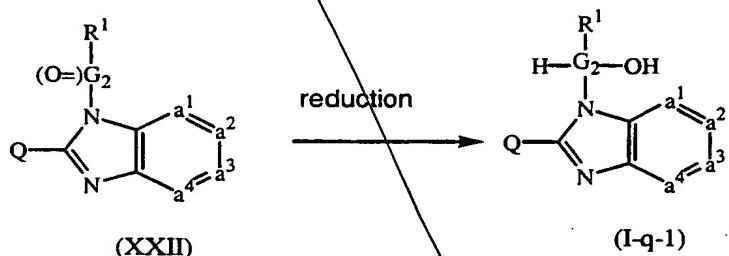
being defined as Q according to claim 1 provided that in the definition of Q, X² is C₂₋₄alkyl-NR⁴, in the presence of a suitable amination agent;

- q) deprotecting an intermediate of formula (XXI)



Sub A¹
5
with R¹, Q, and -a¹=a²-a³=a⁴ defined as in claim 1, and HO-G₁ being defined as G according to claim 1 provided that G is substituted with hydroxy or HO-(CH₂CH₂O)_n;

- r) reducing an intermediate of formula (XXII)



10 with R¹, Q, and -a¹=a²-a³=a⁴ defined as in claim 1, and H-G₂-OH being defined as G according to claim 1 provided that G is substituted with hydroxy and the carbon atom carrying the hydroxy substituent carries also at least one hydrogen, in the presence of a suitable reducing agent.

15 and, if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and, if desired, preparing stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof.

20
25 14. A product containing (a) a compound as defined in claim 1, and (b) another antiviral compound, as a combined preparation for simultaneous, separate or sequential use in the treatment or the prevention of viral infections.

*Sub
A1*

15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredients (a) a compound as defined in claim 1, and (b) another antiviral compound.

*add
A2*